

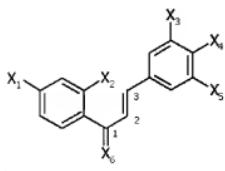
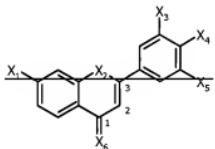
NAJIB et al
Appl. No. 10/520,078
Monday, November 24, 2008
Atty. Ref.: 3665-126
AMENDMENT

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

Claims 1-37. (Canceled)

38. (Currently Amended) ~~A pharmaceutical composition~~ Composition for the treatment or prophylaxis of a pathology related to inflammation, neurodegeneration, deregulations of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system ageing, comprising, in a pharmaceutically acceptable support, at least one substituted 1,3-diphenylprop-2-en-1-one derivative represented by formula (I) below :



(I)

wherein :

X1 represents a halogen or a -R1 group or a group corresponding to the following formula : -G1-R1,

X2 represents a hydrogen atom or a thionitroso group or a hydroxy group or an alkylcarbonyloxy group or an unsubstituted alkyl group or a thiol group or an alkylthio group or an alkylcarbonylthio group, X2 can also represent an oxygen or sulfur atom bound to carbon 3 of the propene chain, so as to form a derivative of the type 2-phenyl-4H-1-benzopyran-4-one or of the type 2-phenyl-4H-1-benzothiopyran-4-one,

X3 represents a -R3 group or a group corresponding to the following formula[[]]:
-G3-R3,

X4 represents a halogen or a thionitroso group or a -R4 group or a group corresponding to the following formula[[]]: -G4-R4,

X5 represents a -R5 group or a group corresponding to the following formula[[]]:
-G5-R5,

X6 is an oxygen atom or a nitrogen atom, in the case where X6 is a nitrogen atom, it carries a hydrogen atom or a hydroxy group or an alkyl group,

R1, R3, R4, R5, which are the same or different, represent a hydrogen atom or an alkyl group substituted or not by a substituent which is part of group 1 or group 2 defined hereinbelow,

G1, G3, G4, G5, which are the same or different, represent an oxygen or sulfur atom,

with at least one of the groups X1, X3, X4 or X5 corresponding to the formula -G-R in which G is a sulfur atom, and

with at least one of the groups R1, R3, R4 or R5 present in the form of an alkyl group containing at least one substituent from group 1 or 2, said alkyl group being

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~~bound directly to the ring or being associated with a group G according to the formula –~~

GR_7

the substituents from group 1 are selected in the group consisting of carboxy groups having the formula[[]]: $-COOR_6$ and carbamoyl groups having the formula[[]]: $-CONR_6R_7$,

the substituents from group 2 are selected in the group consisting of sulfonic acid (SO_3H) and sulfonamide groups having the formula : $-SO_2NR_6R_7$,

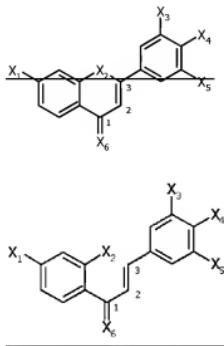
with R_6 and R_7 , which are the same or different, representing a hydrogen atom or an alkyl group possibly substituted by at least one group of type 1 or 2,

with the exception of compounds represented by formula (I) in which[[]]:

X_2 represents a hydrogen atom and X_1 represents $-G1R1$ where $G1$ represents an oxygen atom and $R1$ represents CH_2COOH ,

the optical and geometrical isomers, racemates, tautomers, salts, hydrates and mixtures thereof.

39. (Currently Amended) A pharmaceutical composition Composition for the treatment or prophylaxis of a pathology related to inflammation, neurodegeneration, deregulations of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system ageing, comprising, in a pharmaceutically acceptable support, at least one substituted 1,3-diphenylprop-2-en-1-one derivative represented by formula (I) below :



(I)

wherein :

X1 represents a halogen or a -R1 group or a group corresponding to the following formula[[]]: -G1-R1,

X2 represents a hydrogen atom or a thionitroso group or a hydroxy group or an alkylcarbonyloxy group or an unsubstituted alkylloxy group or a thiol group or an alkylthio group or an alkylcarbonylthio group, X2 can also represent a sulfur atom bound to carbon 3 of the propene chain, so as to form a derivative of the type 2-phenyl-4H-1-benzothiopyran-4-one,

X3 represents a -R3 group or a group corresponding to the following formula[[]]: -G3-R3,

X4 represents a halogen or a thionitroso group or a -R4 group or a group corresponding to the following formula[[]]: -G4-R4,

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X5 represents a -R5 group or a group corresponding to the following formula[[]]:

-G5-R5,

X6 is an oxygen atom or a nitrogen atom, in the case where X6 is a nitrogen atom, it carries a hydrogen atom or a hydroxy group or an alkyloxy group,

R1, R3, R4, R5, which are the same or different, represent a hydrogen atom or an alkyl group substituted or not by a substituent which is part of group 1 or group 2 defined hereinbelow,

G1, G3, G4, G5, which are the same or different, represent an oxygen or sulfur atom,

with at least one of the groups X1, X3, X4 or X5 corresponding to the formula -G-R, and

with none of the groups X3, X4 and X5 representing a hydrogen atom, and

with at least one of the groups R1, R3, R4 or R5 present in the form of an alkyl group containing at least one substituent from group 1 or 2, said alkyl group being bound directly to the ring or being associated with a group G according to the formula -GR₇

the substituents from group 1 are selected in the group consisting of carboxy groups having the formula[[]]: -COOR₆ and carbamoyl groups having the formula[[]]: -CONR₆R₇,

the substituents from group 2 are selected in the group consisting of sulfonic acid (SO₃H) and sulfonamide groups having the formula[[]]: -SO₂NR₆R₇

with R₆ and R₇, which are the same or different, representing a hydrogen atom or an alkyl group possibly substituted by at least one group of type 1 or 2,

with the exception of compounds represented by formula (I) in which[[]]:

X₂ represents a hydrogen atom and X₁ represents -G1R1 where G1 represents an oxygen atom and R1 represents CH₂COOH,

the optical and geometrical isomers, racemates, tautomers, salts, hydrates and mixtures thereof.

40. (Cancelled)

41. (Currently Amended) The composition Composition according to claim 38, wherein none of the groups X₃, X₄ and X₅ represents a hydrogen atom.

42. (Currently Amended) The composition Composition according to claim 38, wherein one or two of the groups X₃, X₄ and X₅ represents a hydrogen atom.

43. (Currently Amended) The composition Composition according to claim 38 or 39, wherein both G1 and G4 represent a sulfur atom.

44. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X₂ is a hydrogen atom, a thionitroso group or a hydroxy group or an alkyloxy or a thiol group or an alkylthio group.

45. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X₄ is a thionitroso group or a -R₄ group or a group corresponding to the formula -G₄-R₄ and X₂ is a thionitroso group or a hydroxy group or an alkyloxy group or a thiol group or an alkylthio.

46. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1 represents a -R1 group or a group corresponding to the formula -G1-R1, where R1 is an alkyl group substituted by a substituent which is part of group 1.

47. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1 is a -G1-R1 group.

48. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1 is a -G1-R1 group in which G1 is an oxygen atom.

49. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1 represents a -R1 group or a group corresponding to the formula -G1-R1, where R1 is an alkyl group substituted by a substituent which is part of group 2 and G1.

50. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X3 represents a -R3 group or a group corresponding to the formula -G3-R3, where R3 is an alkyl group substituted by a substituent which is part of group 1.

51. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X3 represents a -R3 group or a group corresponding to the formula -G3-R3, where R3 is an alkyl group substituted by a substituent which is part of group 2.

52. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X4 represents a -R4 group or a group corresponding to the formula -G4-R4, where R4 is an alkyl group substituted by a substituent which is part of group 1 and G4.

53. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X4 is a -G4-R4 group.

54. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X4 is a -G4-R4 group in which G4 is an oxygen atom.

55. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X4 is a -G4-R4 group in which G4 is an oxygen atom, and X3 or X5 respectively represent R3 or G3R3, on the one hand, and R5 or G5R5, on the other hand, with R3 and R5 being alkyl groups having a substituent from group 1.

56. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X4 represents a -R4 group or a group corresponding to the formula -G4-R4 where R4 is an alkyl group substituted by a substituent which is part of group 2.

57. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1 represents a halogen.

58. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X6 represents an oxygen atom.

59. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1, X3, X4 or X5 represents OC(CH₃)₂COOR₆.

60. (Currently Amended) The composition Composition according to claim 38 or 39, wherein X1, X3, X4 or X5 represents SC(CH₃)₂COOR₆.

61. (Currently Amended) The composition Composition according to claim 38 or 39, wherein the derivative is selected in the group consisting of:

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1-[2-hydroxy-4-carboxydimethylmethyloxyphenyl]-3-[3,5-diter_tbutyl-4-hydroxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-ethyloxycarbonyldimethylmethyloxyphenyl]-3-[3,5-diter_tbutyl-4-hydroxyphenyl]prop-2-en-1-one,
1-[2-hydroxyphenyl]-3-[3-carboxydimethylmethyloxy-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxyphenyl]-3-[3-isopropoxyoxycarbonyldimethylmethyloxy-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3-carboxydimethylmethyloxy-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3-isopropoxyoxycarbonyldimethylmethyloxy-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxyphenyl]-3-[3-carboxydimethylmethyl-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxyphenyl]-3-[3-isopropoxyoxycarbonyldimethylmethyl-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3-carboxydimethylmethyl-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3-isopropoxyoxycarbonyldimethylmethyl-4-hydroxy-5-ter_tbutylphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3,5-dimethoxy-4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one,

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1-[2-hydroxy-4-chlorophenyl]-3-[3,5-dimethoxy-4-isopropoxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,
1-[2-hydroxyphenyl]-3-[3,5-dimethoxy-4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one,
1-[2-hydroxyphenyl]-3-[3,5-dimethoxy-4-isopropoxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-carboxydimethylmethyloxyphenyl]-3-[3,5-di-methoxy-4-hydroxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-isopropoxycarbonyldimethylmethyloxyphenyl]-3-[3,5-dimethoxy-4-hydroxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3,4-dihydroxy-5-carboxydimethylmethyloxyphenyl] prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3,4-dihydroxy-5-isopropoxycarbonyldimethylmethyloxyphenyl]- prop-2-en-1-one,
1-[2-hydroxy-4-carboxydimethylmethyloxyphenyl]-3-[3,5-dimethyl-4-hydroxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-isopropoxycarbonyldimethylmethyloxyphenyl]-3-[3,5-dimethyl-4-hydroxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one,
1-[2-hydroxy-4-chlorophenyl]-3-[3,5-dimethyl-4-isopropoxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,

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1-[2-hydroxyphenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one,

1-[2-hydroxyphenyl]-3-[3,5-dimethyl-4-isopropoxy carbonyl dimethylmethyloxyphenyl]prop-2-en-1-one,

1-[2-hydroxyphenyl]-3-[4-carboxydimethylmethyliophenyl]prop-2-en-1-one,

1-[2-hydroxyphenyl]-3-[4-isopropoxy carbonyldimethylmethyliophenyl]prop-2-en-1-one,

1-[2-hydroxy-4-ethoxycarbonyldimethylmethyloxyphenyl]-3-[3,5-ditertbutyl-4-hydroxyphenyl]prop-2-en-1-one,

1-[2-hydroxy-4-carboxydimethylmethyloxyphenyl]-3-[4-methylthiophenyl]prop-2-en-1-one,

1-[4-chlorophenyl]-3-[3,5-dimethyl-4-tertbutyloxy carbonyldimethylmethyloxyphenyl]prop-2-en-1-one,

1-[4-chlorophenyl]-3-[3,5-dimethyl-4-isopropoxy carbonyldimethylmethyloxyphenyl]prop-2-en-1-one,

1-[4-chlorophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one,

1-[2-hydroxyphenyl]-3-[4-carboxydimethylmethyliophenyl]prop-2-en-1-one,

1-[4-chloro-2-hydroxyphenyl]-3-[4-carboxydimethylmethyliophenyl]prop-2-en-1-one,

1-[4-carboxydimethylmethyloxyphenyl]-3-[3,5-dimethyl-4-hydroxyphenyl]prop-2-en-1-one,

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1-[4-methylthiophenyl]-3-[4-carboxydimethylmethyloxyphenyl]prop-2-en-1-one,
1-[4-carboxydimethylmethyliothiophenyl]-3-[4-methylthiophenyl]prop-2-en-1-one,
1-[2-hydroxy-4-bromophenyl]-3-[3,5-dimethyl-4-
carboxydimethylmethyloxyphenyl]prop-2-en-1-one,
1-[4-carboxydimethylmethyloxyphenyl]-3-[4-methylthiophenyl]prop-2-en-1-one,
1-[4-methylthiophenyl]-3-[3,5-dimethyl-4-
tertbutyloxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,
1-[4-methylthiophenyl]-3-[3,5-dimethyl-4-
isopropyoxy carbonyldimethylmethyloxyphenyl]prop-2-en-1-one,
1-[4-methylthiophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-
2-en-1-one,
1-[2-methoxyphenyl]-3-[3,5-dimethyl-4-
tertbutyloxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,
1-[2-methoxyphenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-2-
en-1-one,
1-[4-hexyloxyphenyl]-3-[3,5-dimethyl-4-
tertbutyloxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,
1-[4-hexyloxyphenyl]-3-[3,5-dimethyl-4-carboxydimethylmethyloxyphenyl]prop-2-
en-1-one,
1-[2-methoxy-4-chlorophenyl]-3-[3,5-dimethyl-4-
tertbutyloxycarbonyldimethylmethyloxyphenyl]prop-2-en-1-one,

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1-[2-methoxy-4-chlorophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethoxyphenyl]prop-2-en-1-one,
1-[4-heptylphenyl]-3-[3,5-dimethyl-4-tertbutyloxycarbonyldimethylmethoxyphenyl]prop-2-en-1-one,
1-[4-heptylphenyl]-3-[3,5-dimethyl-4-carboxydimethylmethoxyphenyl]prop-2-en-1-one,
1-[4-bromophenyl]-3-[3,5-dimethyl-4-tertbutyloxycarbonyldimethylmethoxyphenyl]prop-2-en-1-one,
1-[4-bromophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethoxyphenyl]prop-2-en-1-one.

62. (Withdrawn - Currently Amended) The composition Composition according to claim 38 or 39, wherein the derivative is selected in the group consisting of:

1-[4-methylthiophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethoxyphenyl]prop-2-en-1-one,

1-[4-hexyloxyphenyl]-3-[3,5-dimethyl-4-carboxydimethylmethoxyphenyl]prop-2-en-1-one, and

1-[4-bromophenyl]-3-[3,5-dimethyl-4-carboxydimethylmethoxyphenyl]prop-2-en-1-one.

63. (Cancelled)

64. (Cancelled)

65. (Currently Amended) The composition Composition according to claim 38 or 39, wherein said composition is aimed for the treatment of a pathology related to

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deregulations of lipid and/or glucose metabolism is selected in the group consisting of diabetes, atherosclerosis and obesity.

66. (Canceled)

67. (Cancelled)

68. (Withdrawn - Currently Amended) A method Method of treatment and/or prophylaxis of pathologies related to inflammation, neurodegeneration, deregulations of lipid and/or glucose metabolism, cell proliferation and/or differentiation and/or skin or central nervous system ageing comprising administering to a subject a composition as defined in claim 38 or 39.

69. (New) A method for the treatment of diabetes, atherosclerosis or obesity comprising administering to a subject a composition according to claim 38 or 39.